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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C12Q 1/68		A1	(11) International Publication Number: WO 00/20630
			(43) International Publication Date: 13 April 2000 (13.04.00)
(21) International Application Number: PCT/CA99/00933 (22) International Filing Date: 6 October 1999 (06.10.99) (30) Priority Data: 2,246,623 7 October 1998 (07.10.98) CA (71) Applicant (for all designated States except US): MCGILL UNIVERSITY [CA/CA]; 3550 University Street, Montreal, Quebec H3A 2A7 (CA). (72) Inventors; and (75) Inventors/Applicants (for US only): PELLETIER, Jerry [CA/CA]; 8 Lakeview, Baie D'Urfée, Quebec H9X 3B1 (CA). DAS, Manjula [IN/CA]; Apartment #205, 3484 Stanley, Montreal, Quebec H3A 1S1 (CA). (74) Agents: DUBUC, Jean et al.; Goudreau Gage Dubuc & Martineau Walker, The Stock Exchange Tower, Suite 3400, 800 Place Victoria, P.O. Box 242, Montreal, Quebec H4Z 1E9 (CA).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(54) Title: OLIGONUCLEOTIDE PRIMERS THAT DESTABILIZE NON-SPECIFIC DUPLEX FORMATION AND USES THEREOF			
(57) Abstract			
<p>The present invention relates to the demonstration that a modification of a homopolymeric stretch in an oligonucleotide, or primer, improves the discrimination for binding of such a modified oligonucleotide or primer to its complementary homopolymeric target sequence, as compared to a non-homopolymeric sequence. More specifically, an oligo d(T) primer having two of the thymine bases substituted by 3-nitropyrrole were used in a poly A primed cDNA synthesis experiment to demonstrate an improvement in discrimination between the priming of cDNA synthesis from <i>bona fide</i> poly A sequence as compared to internal A-rich sequences. The present invention relates to modifications of homopolymeric sequences in oligos, decreasing the ridging bonding capacity, in general, since other modifications, such as an oligo d(T) primer substituted with 2' deoxyinosine was also shown to improve the discrimination between the binding to a <i>bona fide</i> poly A tail as compared to A-rich sequences. The present invention thus relates to universal primers which reduce mispriming during cDNA library construction, thereby increasing the proportion of cDNA clones having been primed from the <i>bona fide</i> 3' poly A tail. The present invention further relates to the use of the discriminating oligonucleotides of the present invention in other methods such as mRNA purification, PCR-based detection methods and sequencing.</p>			
<div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;"> <p>m⁷G — Internal A-rich Stretch — Poly (A) Tail</p> <p>UAAAAAAAAAAGAAAAAAAAA — AAAAAAAAAAAAAAAAAA...</p> <p>TTTTTTTTTTTTTTTTTTTT — TTTTTTTTTTTTTTTTTT</p> <p>T_m stable at 37°C -anneals. T_m stable at 37°C -anneals.</p> <p>A</p> </div> <div style="text-align: center;"> <p>Z = 1-(2'-Deoxy-β-D-Ribofuranosyl)-3-Nitropyrrole</p> <p>B</p> </div> <div style="text-align: center;"> <p>Oligo d(T)-Z Primer: 5'-d(T)₁-Z-d(T)₃-Z-d(T)₃-3'</p> <p>C</p> </div> <div style="text-align: center;"> <p>m⁷G — Internal A-rich Stretch — Poly (A) Tail</p> <p>UAAAAAAAAAAGAAAAAAAAA — AAAAAAAAAAAAAAAAAA...</p> <p>TTTTTTTTTTTTTTTTTTTT — TTTTTTTTTTTTTTTTTT</p> <p>T_m unstable at 37°C - does not anneal. T_m stable at 37°C -anneals.</p> <p>D</p> </div> </div>			